Remarks

Claim Objections

The Examiner objected to claims 7-9 because they depended from multiple dependent claim 4. Claim 7 has been amended to remove this dependency. Withdrawal of the objection is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 1-5, 7-10, 12, 15, 21-23, 26-30, 32, 35-36, 38-41, 59, 61-63, 65-67, and 114-118 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 6,440,520, hereinafter "Baglin". The Examiner maintains that the limitations of claim 1 are functional and do not distinguish the claimed device from Baglin and rejected claims 2-5 on the ground that they depend from those functional limitations. Applicants respectfully disagree. Prior to the instant amendment, claim 1 recited that "the magnetic regions have a maximum length, with the maximum length being greater than the maximum width", and Applicants argued that in contrast the regions of Baglin have a circular cross-section and thus do not have a maximum length and a maximum width. The Examiner interpreted the diameter of the base of Baglin's cone-shaped regions as the maximum width and interpreted the measurement along the long axis of Baglin's cone-shaped regions, perpendicular to the substrate, as being the maximum length. Applicants maintain that this interpretation is unreasonable. Baglin repeatedly refers to the measurement along the long axis of the pillar as the height of the pillar and nowhere refers to it as a length. Furthermore, it is customary in the art to refer to the vertical dimension of a three dimensional object as its "height", whereas length and width are horizontal dimensions. The instant specification clearly distinguishes between length and width, which are horizontal dimensions measured parallel to the surface of the substrate, and height, which is a vertical dimension measured in a direction perpendicular to the surface of the substrate. While Applicants continue to maintain that the device of claim 1 as presented in the previous office action is clearly distinct from the device of Baglin, in the interests of furthering prosecution claims 1 and 3 have been amended to indicate that the magnetic regions have a maximum length parallel to the surface of the substrate and a maximum width parallel to the surface of the substrate, with the maximum length being greater than the maximum width. Claim 1 has also been amended to provide

antecedent basis for the word "surface". Support for the amendments is found throughout the specification, e.g., from page 21 line 22 to page 22 line 3 of the application as filed, referring to the length and width as being in the x and y directions, in Figure 2, which shows an exemplary device from above and indicates the x and y directions, and Figure 4, which shows a perspective side view of adjacent regions and clearly indicates the x and y directions parallel to the surface of the substrate and the z direction (height), perpendicular to the surface of the substrate. Applicants note Baglin's comment that the elevated features are somewhat irregular in shape. Nevertheless, Baglin repeatedly refers to the width of the base of the pillars as their "diameter", and there is nothing to suggest that the pillars could reasonably be considered to have a length and a width. Furthermore, since any deviations from symmetry associated with the irregular shape would be randomly oriented with respect to each other and with respect to adjacent pillars, they would tend to cancel each other out. Thus even if Baglin's pillars could be considered to have a length and width, the shape of Baglin's regions and their orientation with respect to each other would not have sufficient directionality to generate localized magnetic fields between adjacent regions sufficient to trap a magnetic particle as in the instantly claimed invention. In contrast, as is evident from the instant specification and figures and is inherent in original claim 1, adjacent magnetic regions of the instantly claimed invention are so aligned along the direction of their maximum length that they generate a localized magnetic field within the gap between adjacent regions sufficient to trap a magnetic particle (see, e.g., Figures 2, 3, and 4, 12, and 14). To make this distinction from Baglin's device more explicit, claim 1 has been amended to recite that the adjacent magnetic regions are so aligned with one another in the directions of their maximum length that the localized magnetic fields are sufficient to trap a magnetic particle between adjacent magnetic regions with a trapping energy at least three times greater than the thermal energy of the particle at room temperature. Applicants submit that Baglin does not teach or suggest such a configuration. Withdrawal of the rejection of claims 1 and 2 is respectfully requested.

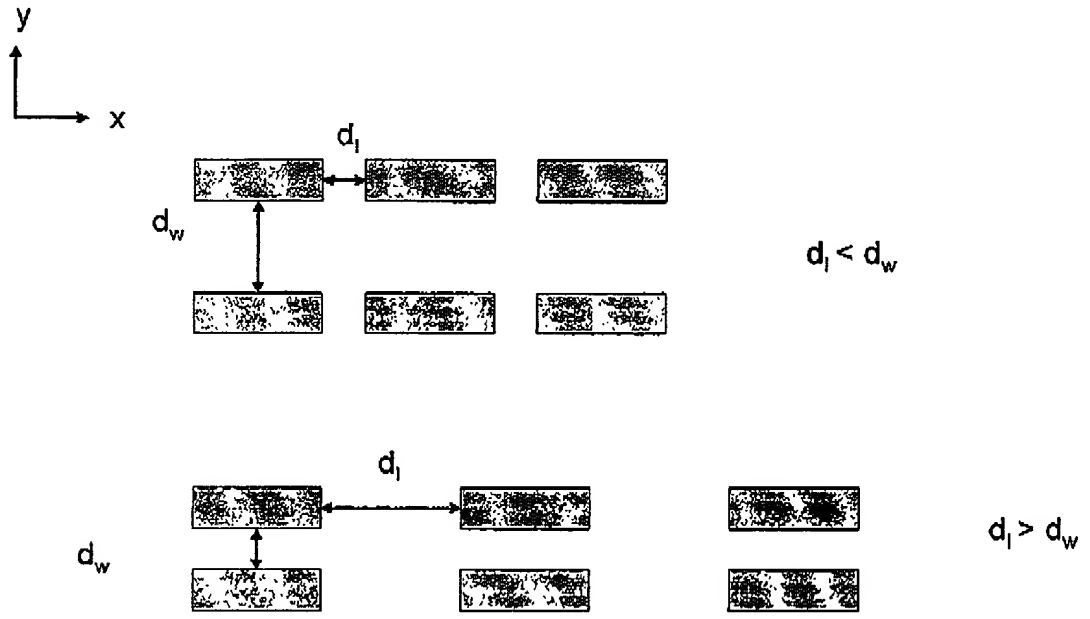
The Examiner rejected claims 3 on the ground that it depends on the functional limitations of claim 1. Applicants respectfully disagree. Claim 3 is an independent claim and recites structural features of the claimed device that are not found in claim 1 and clearly distinguish the claimed device from that of Baglin. The Examiner appears to overlook these features. Claim 3 recites that the device comprises a plurality of regions are spaced apart along the dimension of the maximum length and a plurality of regions are spaced apart along the dimension of the maximum

width, so that the distance separating adjacent regions in the dimension of the maximum length is less than the distance separating adjacent regions in the dimension of the maximum width. *Baglin does not teach such a configuration.* The Examiner's attention is directed to Applicants' remarks below addressing the rejection claim 59 for further discussion. Withdrawal of the rejection is respectfully requested.

Claim 5 recites that the magnetic regions are appropriately shaped and have an appropriate size so as to generate localized magnetic fields that exist substantially in a volume between adjacent north and south poles of adjacent magnetic regions above and parallel to the upper surface of the device. Baglin does not teach magnetic regions having such shapes and sizes. To further point out the structural distinction between the pillars of Baglin and the device of claim 5, the claim has been amended to recite that adjacent magnetic regions have ends with opposite magnetic polarities facing each other across a gap between them. Support for the amendment is found from page 21 line 22 to page 22 line 3 of the application as filed. Baglin does not describe a device comprising adjacent magnetic regions having ends with opposite magnetic polarities facing each other across a gap between them. Withdrawal of the rejection is respectfully requested.

With respect to claim 59 the Examiner contends that since the array of Baglin is positioned in columns and rows and the claimed array is also arranged in columns and rows, the magnetic regions of Baglin are also spaced apart along the dimension of the maximum width and the dimension of the maximum length and the distance separating adjacent regions in the dimension of the length is less than the distance separating adjacent regions of (*sic*) the dimension of the width. Applicants respectfully disagree for each of the following reasons. First, claim 59 says nothing about rows and columns and even if it did, whether the magnetic regions of the claimed device are arranged in columns and rows is simply not relevant to the question of whether Baglin's device possesses the claimed features with respect to spacing between the regions. Second, in rejecting claim 1, the Examiner indicated that the axis of the cone is the maximum length of Baglin's regions (office action, page 13). Baglin's regions are clearly not spaced apart along the dimension of the axis of the cone. Third, the fact that an array of regions that have a maximum length and maximum length is arranged in columns and rows does not mean that the distance separating adjacent regions in the dimension of the length is necessarily less than the distance separating adjacent regions in the dimension of the width. For example, in the figure below both arrays are arranged in rows and columns. The x direction is the direction of the

maximum length for both arrays. The y direction is the direction of the maximum width for both arrays. d_l is the distance between the regions in the direction of their maximum length. d_w is the distance between the regions in the direction of their maximum width. In the upper array, $d_l < d_w$ as recited in claim 59. However, in the lower array $d_l > d_w$. Thus the fact that an array is arranged in rows and columns says nothing about the separation of the array elements in the direction of their maximum length and maximum width. Withdrawal of the rejection of claim 59 is requested for this additional reason.



Claims 7-10, 12, 15, 21-23, 26-30, 32, 35-36, 38-41, 61-63, and 65-67 depend from claims 1, 3, and/or 59. Since claims 1, 3, and 59 are clearly distinct from the device of Baglin, withdrawal of the rejection of claims dependent therefrom is respectfully requested.

Claims 1-5, 10-12, 21-23, 26, 30, 31, 33, 34, 35, 38-41, 45, 46, 48, 49, and 54-58 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,395,498, hereinafter "Gombinsky". Gombinsky teaches a magnetic matrix in which 4 magnets are separated from each other by strips of rubber to form alternating layes. The Examiner states that the rubber layers in the alternating layers of magnets and rubber taught by Gombinsky are gaps. Claims 1 and 5 have been amended to recite that and the gaps are available for fluid flow among

them and for occupancy by magnetic particles prior to introduction of magnetic particles to the device so that forces generated by the localized magnetic fields between adjacent regions can trap magnetic particles in the gaps between them. Support for the amendment is found throughout the specification. See, e.g., from page 44 line 1 to page 45 line 20 of the application, as filed. Thus the gaps cannot be filled with rubber that is an integral part of the device as in Gombinsky's magnetic matrix. Withdrawal of the rejection of claims 1, 5, and claims dependent thereon is respectfully requested.

Claim 3 recites that the device comprises a plurality of regions spaced apart along the dimension of the maximum length and a plurality of regions spaced apart along the dimension of the maximum width, so that the distance separating adjacent regions in the dimension of the maximum length is less than the distance separating adjacent regions in the dimension of the maximum width. The Examiner asserts that the array of Gombinsky and the claimed array are positioned in columns and rows and that Gombinsky's array therefore possesses the claimed features. Applicants respectfully disagree for each of the following reasons. Firstly, whether the claimed array is arranged in columns and rows is simply not relevant to the question of whether Gombinsky's device possesses the claimed features with respect to spacing between the regions. Secondly, Gombinsky does not teach an array arranged in rows and columns. Gombinsky teaches planar magnets, pairs of magnets, or a device consisting of magnets separated by rubber strips which at most has rows of magnetic regions. Gombinsky teaches that the magnetic particles can be uniformly distributed or distributed in vertical, horizontal, or diagonal strips (col. 7, line 56-col. 8, line 12). The Examiner concedes that, "the pattern of spots in the array is simple rows of lines" (Office Action, page 5). Thus Gombinsky does not describe an arrangement of rows and columns. Applicants note that the arrangements of magnetic particles in Figure 3b and 4 were produced using a planar magnet and a net rather than a device having magnetic regions arranged in rows and columns (see col. 7, lines 19-35) and simply shows a grid superimposed on a matrix of magnetic particles. Furthermore, as discussed above, even if Gombinsky's array was arranged in columns and rows this alone does not imply anything about the distance separating adjacent regions. If the Examiner maintains the rejection of claim 3 as being anticipated by Gombinsky, Applicants respectfully request that the Examiner point out the teachings in Gombinsky on which the rejection of claim 3 is based.

Claim 10 recites that the magnetic material regions are arranged in a pattern of mutually perpendicular rows and columns. As discussed above, Gombinsky does not teach such a pattern. If the Examiner maintains the rejection of claim 10 as being anticipated by Gombinsky, Applicants respectfully request that the Examiner specifically point out where Gombinsky teaches magnetic material regions arranged in a pattern of mutually perpendicular rows and columns.

Claim 21 has been amended and now recites that adjacent magnetic regions are separated by a gap approximately equal in size to the size of a magnetic particle having a largest dimension of less than approximately 200 μm. Support for the amendment is found page 11 lines 4-7 of the application as filed. The gaps taught by Gombinsky are all clearly on a much larger in size in keeping with the fact that Gombinsky's device is intended for use in the context of conventional gel electrophoresis.

Claim 26 depends on claim 25, which was not rejected as being anticipated by Gombinsky. Applicants submit that the rejection of claim 26 should be withdrawn.

Claim 122 stands rejected under 35 U.S.C. § 102(a) as being anticipated by U.S. Pat. No. 6,331,365 (hereinafter "Baglin 2"). Claim 122 has been amended to recite that the magnetic regions project above the surface of the substrate. Support is found throughout the specification. Baglin 2 teaches a horizontal magnetic recording medium (col. 2, lines 59-64; see also the Figures). Accordingly Baglin's magnetic regions do not project above the surface of the substrate. Withdrawal of the rejection is respectfully requested.

Claim 123 stands rejected under 35 U.S.C. § 102(a) as being anticipated by U.S. Pat. No. 4,397,560, hereinafter "Andresen". Andresen teaches a photometer for sensing the optical density of liquids located in wells of a microtray by means of a *single* photodetector. See col. 3, lines 15-27, and note the use of the singular word "photodetector". See also Figures 2 and 3, showing a single photodetector. See also col. 1, lines 55-65, and claim 1, which clearly indicate that the microtray is to be moved in relation to the single light source and photodetector so as to sequentially position different wells between the light source and photodetector. Thus Andresen does not teach or suggest a plurality of photodetectors as recited in claim 123. Furthermore, there is no motivation to modify the device of Andresen comprising magnetic sensors to include a plurality of photodetectors. Since there is only a single light source, additional photodetectors would provide no benefit relative to the configuration with a single photodetector. The reason for having the magnetic sensors is to allow identification of the specific well that is positioned where

its contents can be detected by the single light source and photodetector as the microtray is moved relative to the fixed position of the light source and photodetector. A device comprising a plurality of light sources and photodetectors and light sources would not need the magnetic sensors. Withdrawal of the rejection is respectfully requested.

Claim 124 stands rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 6,432,630, hereinafter "Blankenstein". Claim 124 has been amended to recite that the channels are positioned in communication with the magnetic regions so as to allow introduction of fluids to the magnetic regions via the channels so that the fluids contact the magnetic regions following introduction of the fluids via the channels. Support for the amendment is found in from page line 13 to page 39 line 11 of the application as filed, which explain use of the channels to introduce a fluid sample containing magnetic particles to the array of magnetic islands on the chip and to remove the particles following data collection, clearly indicating that the fluids are in contact with the magnetic regions following introduction of the fluids to the magnetic regions. Blankenstein teaches the use of magnetic fields to separate particles or cells stained with particles, wherein the particles or cells are located in a flow channel. The magnetic field may be generated using magnets. Blankenstein does not teach a device in which the channels are in communication with the magnets. Instead, the magnets are physically separated from the interior of the flow channel so that the fluids do not contact the magnets. Figure 13 clearly shows that fluid channel 5 is adjacent to and separated from magnets 8 by solid material indicated with hatch markings. Col. 19, lines 60-67, indicates that the magnets and flow channels are located on separate cartridges with the magnets located below the flow channel. For these reasons, Applicants submit that Blankenstein does not teach the claimed invention. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 16-20 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Baglin or Gombinsky. While not agreeing that it would have been obvious to modify the device of Baglin or Gombinsky to include at least 1000; 10,000; 100,000; 250,000; or 1,000,000 magnetic regions per centimeter squared, Applicants respectfully submit that even had it been obvious to modify the device of Baglin or Gombinsky as suggested by the Examiner, the instant amendments would still clearly distinguish the claimed device from the device that would result from making such modifications to the device of Baglin or Gombinksy. Therefore, the rejection for obviousness

should be withdrawn. Furthermore, the teachings of *In re Boesch*, 617 F.2d 272 (CCPA 1980), are not applicable to the instant situation for each of the following reasons. *In re Boesch* involved selecting the composition of an alloy where the prior art disclosed a broad range, the claims at issue recited a narrower range within this broad range, and the prior art suggested the direction of experimentation to achieve a desired result. In contrast, the instant claims do not recite a narrower range within a broad range taught by Baglin or Gombinsky where the prior art suggests the narrower range. Second, the Examiner quoted only part of the holding mentioned in *In re Boesch*; the complete sentence reads, "This accords with the rule that discovery of an optimum value of a result effective variable *in a known process* is ordinarily within the skill of the art." (italics added) *In re Boesch*, at 276. Thus the relevant question in reference to *In re Bosch* is whether the number of magnetic regions recited in the instant claims is a result effective variable in a process taught by Baglin or Gombinsky such that it would be obvious to modify Baglin or Gombinsky as suggested by the Examiner. Applicants submit that the answer is "no". While the number of magnetic regions recited in claims 16-20 may be appropriate for the process performed by the device of claims 16-20, there is nothing to suggest that these values would be optimum for the process performed by the devices of Baglin or Gombinsky. Baglin does not teach a process for forming an array of magnetic particles. Gombinsky teaches making a matrix of magnetic particles to capture species of biological macromolecules from a gel following gel electrophoresis. There is nothing in Gombinsky to suggest that modifying his device to include at least 1000; 10,000; 100,000; 250,000; or 1,000,000 magnetic regions per centimeter squared would optimize the process. Instead, it would greatly reduce the size of the regions, making them smaller than the macroscopic dimensions of the lanes and bands in a gel electrophoresis experiment and making it hard to recover the particles using the process taught by Gombinsky.

Claims 113 and 119-121 also stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Baglin or Gombinsky. While not agreeing that it would have been obvious to modify the device of Baglin or Gombinsky as suggested by the Examiner, Applicants respectfully submit that even had it been obvious to so modify the device of Baglin or Gombinsky, the instant amendments would still clearly distinguish the claimed device from the device that would result from making such modifications. In addition, claim 121 recites that the magnetic regions project above the surface of the substrate, which is not taught or suggested by Gombinsky. Therefore, the rejection for obviousness should be withdrawn. Furthermore, as discussed above, *In re Boesch* is

not applicable to the instant situation. Neither Baglin nor Gombinsky teaches or suggests a process that involves trapping magnetic particles within gaps; therefore it would not have been obvious to modify Baglin or Gombinsky to achieve such a result. Neither Baglin nor Gombinsky teaches processes that are optimized by selecting magnetic regions having the maximum lengths and maximum widths recited in the instant claims. Neither Baglin nor Gombinsky teaches processes that are optimized by selecting magnetic regions having the distances between their ends as recited in the instant claims. Neither Baglin nor Gombinsky teaches broad ranges of which the instant claims carve out a narrower range as in *In re Boesch*. For each of these reasons, withdrawal of the rejection is respectfully requested.

Claims 47 and 50-53 stand rejected under U.S.C. § 103(a) as being unpatentable over Gombinsky in view of U.S. Pat. No. 6,355, 491, hereinafter "Zhou". These claims all depend from claim 1. Applicants respectfully submit that even had it been obvious to modify Gombinsky's invention as suggested by the Examiner, the instant amendments would still clearly distinguish the claimed device from the device that would result from making such modifications to Gombinksy's invention. Therefore, the rejection for obviousness should be withdrawn.

Claim 43 stands rejected under U.S.C. § 103(a) as being unpatentable over Gombinsky in view of Andresen. Claim 43 recites the device of claim 1, further comprising a plurality of photodetectors located in proximity to locations for trapping the magnetic particles so as to detect an optical signal from trapped particles. Applicants submit that even if it had been obvious to modify Gombinsky's device to include photodetectors in proximity to regions for trapping magnetic particles, the amendment to claim 1 clearly distinguishes the claimed device from the device that would result from including photodetectors in Gombinsky's device. Furthermore, as discussed above, Andresen does not teach or suggest a plurality of photodetectors located in proximity to locations for trapping magnetic particles. Thus there is no teaching in Andresen that would suggest modifying the device of Gombinsky to include a plurality of photodetectors located in proximity to locations for trapping magnetic particles. Therefore, the combination of Gombinsky and Andresen cannot render claim 43 obvious. Withdrawal of the rejection is respectfully requested.

Claim 44 stands rejected under U.S.C. § 103(a) as being unpatentable over Gombinsky in view of Blankenstein. Claim 44 recites the device of claim 1, further comprising a microfluidic assembly. Applicants submit that even if it had been obvious to modify Gombinsky's device to

include a microfluidic assembly, the amendment to claim 1 clearly distinguishes the claimed device from the device that would result from including a microfluidic assembly in Gombinsky's device. Furthermore, claim 44 has been amended to recite that the microfluidic assembly comprises channels positioned in communication with the magnetic regions so as to allow introduction of fluids to the magnetic regions via the channels so that the fluids contact the magnetic regions following introduction of the fluids via the channels. As discussed above, Blankenstein does not teach a device in which the channels are in communication with the magnets. Thus the combination of Gombinsky and Blankenstein cannot render the claimed invention obvious. Withdrawal of the rejection is respectfully requested.

New claim

New claim 125 recites a device for forming an array of magnetic particles, the device comprising a substrate comprising a plurality of magnetic regions, wherein the substrate comprises a surface, and wherein the localized magnetic regions produce a plurality of localized magnetic fields concentrated in gaps between the regions, and wherein the magnetic regions project above the surface of the substrate and have a maximum length parallel to the surface and a maximum width parallel to the surface, wherein the maximum length is between 3 and 5 times as great as the maximum width or between 5 and 10 times as great as the maximum width. This claim includes features found in claims 113 and 121 and is similarly supported as well as being novel and non-obvious in view of Baglin and Gombinsky.

In conclusion, in view of the amendments and remarks presented herein, the application and pending claims comply with the requirements of 335 U.S.C. §102 and §103. Applicants therefore respectfully submit that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful in resolving any remaining issues, the undersigned would appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5000.

A check in the amount of $510.00 to cover the fee for a three (3) month extension of time is enclosed. Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully Submitted,
CHOATE, HALL & STEWART LLP

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Brenda Herschbach Jarrell, Ph.D.
Registration No. 39,223

PATENT DEPARTMENT
CHOATE, HALL & STEWART LLP
Two International Place
Boston, Massachusetts 02110
Telephone: (617) 248-5000
Facsimile: (617) 248-4000